REMARKS

Reconsideration is requested.

Claims 1-34, 37-42, 50 and 54-57, have been canceled, without prejudice. Claims 68-71 have been added. The claims have been revised, without prejudice. Support for the amended claims may be found, for example, on page 1, lines 6-10; page 3, lines 3-5, 16-20 and 24-25; the Figures and experimental section of the description, such as pages 25-28. No new matter has been added. These amendments are made without prejudice or disclaimer and solely in order to facilitate reconsideration of this application. In particular, applicant reserves his right to file a continuation and/or divisional application at a later stage, and the present amendment shall not be considered as an admission of the objection or as a waiver of any subject matter.

The objection to claim 58 is obviated by the above amendments. Withdrawal of the objection is requested.

To the extent not obviate by the above amendments, the Section 112, first paragraph "enablement", rejection of claims 35, 36, 43-46, 54-58 an 64-67, is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

The claims are supported by an enabling disclosure.

The objected-to term "suitable" has been further deleted from the rejected claims in response to the Examiner's comments. Moreover, claim 54 has been canceled, without prejudice. Further, the claims are directed to plasmids and recombinant viral vectors, as described by the specification.

Withdrawal of the Section 112, first paragraph "enablement" rejection is requested.

To the extent not obviated by the above, the following rejections are traversed:

the Section 103 rejection of claims 35, 36 and 46 over Barry (Human Gene Therapy 12:1103-1108; 2001), in view of Paulding (JBC 274:2532-2538);

the Section 103 rejection of claim 43 over Barry and Paulding and Ramezani (Mol. Ther. 2:458-469; 2000);

the Section 103 rejection of claims 40, 44, 64 and 65 over Barry, Paulding, Ramezani and Rogers (JBC 274:6421-6431; 1999);

the Section 103 rejection of claims 41, 42, 45-51, 66 and 67 over Barry, Paulding, Ramezani, Rogers and Aronov (Journal of Molecular Neuroscience, 12:131-145; 1999); and

the Section 103 rejection of claims 52, 56 and 59 over Barry view of Chang (Curr. Gene Ther. 2:237-251; 2001).

Reconsideration and withdrawal of the Section 103 rejections are requested in view of the above and the following distinguishing comments.

The applicants have previously noted deficiencies in the primary reference and demonstrated a synergistic effect from the claimed invention. The applicants urge the Examiner to appreciate

that an unexpected property of the product (i.e., a synergistic effect) is evidence of its unobviousness. See In re Albrecht, 198 USPQ 208 (CCPA 1978).

The applicants have tested combinations of these posttranscriptional regulatory elements and unexpectedly found that they could cooperate or act in synergy to provide positive effects on transgene expression. This is confirmed by the declaration form Dr Jacques Mallet, inventor, and by the Brun *et al.* reference, of record. The applicants submit that the cited combination of art would not have suggested the vector according to the claimed invention not its effect in enhancing expression of the transgene.

The Examiner is understood to not be persuaded by the Declaration evidence that the Central Polypurine Tract (cPPT) is not a posttranscriptional regulatory element. See the Declaration of Jacques Mallet indexed in the PTO IFW on January 31, 2008. The Examiner is urged to appreciate that the declarant is a specialist in the construction of lentiviral vectors and has provided evidence in the Declaration based on scientific articles published in reviewed journals. As stated on page 2 of the Declaration, the "cPPT sequence" used by Barry et al. is the "flap sequence" or "HIV-1 DNA flap nuclear transporter" used by Zennou et al.. In addition to the Declaration of record, the applicants believe this distinction is confirmed by Barry et al. which states as follows: *"The incorporation of a central polypurine tract (cPPT) (Charneau and Clavel, 1991; Follenzi et al., 2000;* ***Zennou et al., 2000)****..."* (see left column, lines 8-9, page 1104 of Barry et al.). As also noted in the Declaration, the cPPT sequence increases the vector transduction efficacy by about 10 fold, due to the stimulation of the genome vector nuclear import [see Zennou *et al.*, 2001 (naming in particular Dr. Jacques Mallet as author), 2001, page 448, right column, and Zennou *et al.*, 2000, page 180, Figure 6B].

The comparison and analysis of Dr Jacques Mallet in the evidence of record is thus to be considered by the Examiner as a confirmation of the advantageous additional synergistic effects produced by the vectors according to the present invention which comprise **at least two distinct postranscriptional regulatory elements** functional in mammalian cells, **each comprising** a **UTR region of a eukaryotic mRNA selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR.**

It is further to be noted that cPPT, even if considered to be a post transcriptionnal regulatory element, is not a post transcriptionnal regulatory element comprising a UTR region of a eukaryotic mRNA, as claimed.

The applicant further note that the additional synergistic effects on transgene expression are clearly demonstrated in the experimental part of the application as filed wherein the claimed vectors have been tested and specific combinations of postranscriptional regulatory elements have been validated for particular cell types, namely glial cells, fibroblasts and neuronal cells. These methods are described in new claims 68-71.

Withdrawal of the Section 103 rejections is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /B. J. Sadoff/
B. J. Sadoff
Reg. No. 36,663

BJS:
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100